Available online at www.sciencedirect.com

ScienceDirect

APCBEE Procedia 9 (2014) 42 – 47

Procedia APCBEE

www.elsevier.com/locate/procedia

ICBEE 2013: September 14-15, New Delhi, India

Influence of Substituents on Reactivity and Reaction Mechanism of S_N Reaction of Some Organophosphorus Compounds; Relied on Linear Free Energy Relationship

Bilkis Jahan Lumbiny[a,]*, Zhang Hui[b] and M. Azizul Islam[c]

[a,c]*Department of chemistry, University of Rajshahi, Rajshahi 6205, Bangladesh.*
[b]*Department of Chemistry, Inha University, Incheon 402-751, South Korea.*

Abstract

The tetracoordinated organophosphorous compound (4 - Chlorophenyl 4 - methyl phenyl Chlorophosphate, 1) were synthesized, characterized and nucleophilic substitution reaction (pyridinolysis) were investigated in acetonitrile at 5.0 ^{o}C by varying substituents in nucleophiles. The reactivity is expressed in terms of second-order rate constant, k_2 and measured conductometrically. Physical organic chemistry tools mainly Hammett (ρ), Brönsted (β) Linear Free Energy Relationship (LFER) coefficients being determined in quest for the mechanistic information by comparing pyridinolysis of structurally similar organophosphorous compounds reported earlier. Nice linear correlation being found for Hammett ($\log k_2$ vs σ_X) and Brönsted ($\log k_2$ vs $pK_{a(X)}$) plots. In the light of the reported results the LFER obtained for 1 with negative value of the ρ_X , −5.78 and large positive value for β_X , 1.17 can be interpreted as S_N2 process, with greater extent of bond formation in TS of 1.

Selection and peer review under responsibility of Asia-Pacific Chemical, Biological & Environmental Engineering Society

Keywords: ORGANOPHOSPHOROUS COMPOUNDS, PYRIDINOLYSIS, REACTIVITY, HAMMETT (ρ) AND BRÖNSTED (β) LFER, REACTION MECHANISM, TS STRUCTURE

* Corresponding author. Tel.:+ 88-01737227841; fax.+88-0721750064
E-mail address: blksjahan@yahoo.com.

Selection and peer review under responsibility of Asia-Pacific Chemical, Biological & Environmental Engineering Society
doi:10.1016/j.apcbee.2014.01.008

1. Introduction

The mechanism of a chemical reaction can be interpreted using Linear Free Energy Relationship (LFER) [1]. This is an empirical observations by which the shapes of the potential energy surfaces (PES) of a reaction are not substantially altered by varying the substituents [1]. Phosphoryl transfer and related reactions withdraw interest with many opportunities for research or application development especially due to its relevance to biological chemistry as well as its usefulness as agricultural chemicals like pesticides, oil and gasoline additives, etc. [2]. A library of new organophosphors compounds being synthesized and series of kinetics and mechanism of nucleophilic substitution reactions on phosphoryl group (P=O) and thiophosphoryl group (P=S) have been reported for long from the research group acknowledged [2-9]. The above studies being relied on physical organic chemistry methods; Hammett and Brönsted LFER, cross interaction constants (CICs), heavy atom kinetic isotope effects (KIE) which have provided unambiguous evidence for the interpretation of the mechanistic pathway. It has been reported that nucleophilic substitution at a (thio)phosphoryl (P=S/O) center generally proceeds either through stepwise mechanism with a trigonal bipyramidal pentacoordinated (TBP-5C) intermediate (upper route, Fig. 1) or an S_N2 mechanism with TBP-5C transition state (TS) (lower route, Fig. 1) [2-9]. Our very recent studies showed that in case of concerted mechanism the nucleophile can approach towards reaction centre in two different ways. A hydrogen-bonded, four-center type TS is suggested for a frontside attack while the TBP-5C TS is suggested for a back-side attack as shown in Fig. 2 [3, 5, 9].

This is also very strongly claimed from previous studies as the substituents around the P centre (leaving or nonleaving group), or substituents around nucleophilic centre varies, the reactivity, selectivity, finally mechanistic pathway for S_N reaction varies a lot. In the present study the tetracoordinated organophosphorus compound 4-Chlorophenyl 4-methyl phenyl chlorophosphate [4-ClPhOP(=O)(4-MePhO)Cl], 1**,** being synthesized, characterised by spectrometric methods and Element Analysis. Then aminolyses reaction with tertiary amine, substituted pyridines have been carried out at 5.0 ^{o}C in acetonitrile (Fig. 3). Recently the pyridinolysis of some structurally similar organophosphorus compounds, *O*-aryl phenyl phosphonochloridothioates [PhP(=S)(OPh-Y)Cl, 2, and *O,O*-diphenyl *Z*-*S*-phenyl phosphorothiolates [$(PhO)_2P(=O)(S\text{-}Ph\text{-}Z)$], 3, in acetonitrile at 35.0 ^{o}C, were observed by varying substituents around phosphorus centre (Y in 2, Z in 3) or in nucleophile (X) and extended to pyridinolysis of 4-Chlorophenyl phenyl chlorophosphate [4–ClPhOP(=O)(OPh)Cl], 4, in acetonitrile at 5.0 ^{o}C. The reported mechanism according to LFER is S_N2 without any change in mechanism for the system 2 and 4, but for 3 a change in mechanism is interpreted at Z = H from concerted to stepwise with rate-limiting expulsion of the leaving group [2, 4, 9]. Comparing the reactivities, the linear free energy selectivity parameters with the above comparable systems this study could be a further evidence in support of the above mechanism, and also to assess the influence of the variable substituents on TS and the reaction mechanism as well.

2. Experimental

GR grade starting materials (4-Chlorophenyl dichlorophosphate, 4-methyl phenol, Triethyl amine) substitued pyridines were purchased and used. HPLC grade acetonitrile (less than 0.005% H_2O content) were used to prepare nucleophile solution to study.

Synthesis and characterization:

Equimolar proportion of the starting materials were taken with methylene chloride and stirred in ice bath for 2 hrs. The compound 1 is obtained from the reaction mixture by column chromatography and characterized in the following way.

Colourless liquid; IR (neat, cm^{-1}) 3098 (C–H, aromatic), 2925 (-CH_3 Asym), 2867 (-CH_3 Sym), 1311

(P=O.), 1209, 1186, 1163 (C-O-Ar), 1093, 975, 832 (P-O-Ar str); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (dd, J = 8.8Hz, 0.8 Hz, 2H), 7.25 (dd, J = 9.2, 1.6Hz, 2H), 7.19-7.17 (m, 4H), 2.36 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$), 148.26, 147.58, 136.39, 132.97, 130.53, 130.09, 121.85, 120.06, 21.78 (CH_3), ^{31}P NMR (162 MHz,$CDCl_3$) δ 0.46 (s, 1P); m/z, 316 (M^+); Anal. Calcd for $C_{13}H_{11}O_3PCl_2$: C, 49.24; H, 3.50; Found: C, 49.16; H, 3.72;

Kinetics [2, 3, 4, 5, 6, 7, 8, 9]:

Reactions were carried out under pseudo first-order conditions at 5.0 ^{o}C in which amine concentrations were at least 20 times greater than the substrate concentration. Thus the pseudo first- order rate (k_{obsd}) was obtained experimentally by using Guggenheim equation (eq. 1) by nonlinear curve fitting method in ORIGIN program.

$$\lambda_t = \lambda_\infty - (\lambda_\infty - \lambda_0)e^{(-kobsd \times t)} \ldots \quad (1)$$

[where, λ_0 = initial conductivity, λ_t = conductivity at any time, λ_∞ = conductivity at infinity]

This will ultimately produce second-order rate constant (k_2) from the slope of the plots (see Table 1) of k_{obsd} vs [Nu], in eq. 2, which gave very good linearity in all cases (regression > 0.997).

$$k_{obsd} = k_0 + k_2 [Nu] \ldots \quad (2)$$

3. Tools to interprete mechanism (theory)

In the early part of twentieth century the quantitative study of LFER was introduced by the Danish scientist Johannes Nicolaus Brönsted (1923) and Swedish scientist Louis Plack Hammett (1937).

Hammett Equation [1, 10]:

It treats the electronic effect of substituents on the rate of equilibria of organic reactions, can be expressed as follows equation 3(a) and 3(b)

$$\log (k_X/k_H) = \sigma\rho \ldots (a) \quad or \quad \log (K_X/K_H) = \sigma\rho \ldots (b) \quad (3)$$

k_X or K_X is the rate or equilibrium constant, respectively, for the given reaction of m- or p-XC_6H_4COOH, k_H or K_H refers to the reaction of C_6H_5COOH, i.e., X = H, σ is the substituent constant, ρ is the reaction constant or Hammett coefficients and obtained by plotting $\log k_2$ vs. σ_X.

Significance of Sign and Magnitude of ρ: the susceptibility of the reaction to substituents, (+ve) sign; a reaction favored by EWS and $\rho < 1$ indicates negative charge is built, (–ve) sign and $\rho > 1$ suggest reverse situation.

The Brönsted equation [11] :

The Gibbs free energy for proton dissociation is proportional to the activation energy (eq. 4a, 4b) for the catalytic step. When the relationship is not linear, the chosen group of catalysts do not operate through the same reaction mechanism.

$$k_b = G_b K_b^{\beta} = G_b (K_W/K_a)^{\beta} = G_b K_a^{-\beta} \quad \ldots (a) \quad or \quad \log k_b = \beta p K_a + Constant \ldots\ldots (b) \quad (4)$$

The Brönsted correlations of rate constants with nucleophile pK_a (β_X) is one measure of the degree of nucleophile bond formation in the rate determining TS. Reactions that have low values for proportionality constants (β_X) are considered to have a transition state closely resembling the reactant with little proton transfer, with a high value, resembles product .

4. Results and Discussion

The second-order rate constants ($k_2 \times 10^3/M^{-1}s^{-1}$) of the pyridinolysis 1, [4-ClPhOP(=O)(4-MePhO)Cl], 2,

with Y = H: (PhO)PhP(=S)Cl, 3 with Y = H: $(PhO)_2P(=O)SPh$, 4: (4–ClPhO)PhOP(=O)Cl obey the following order of reactivity respectively (see Table 1)

3 (P=O, 44.2) > 4 (P=O , 31.6) > 1(P=O , 26.2) > 2 (P=S, 11.2)

At a glance, the reaction rates seem to be proportional to the positive charge on reaction center P. However, it is well known that P=O substrates are more reactive than P=S because of electronegativity difference between O and S, favoring O over S. Also the presence of electron donating substitent, 4-Me in 1 retards the rate of reaction than that of 4 follow the expected trend.

The Hammett plots for substituent (X) variations in the nucleophile (log k_2 vs. σ_X, Fig. 4) and Bronsted plots (log k_2 vs. pK_a(X*)*, Fig. 5) show linearity for 1, same as 2, 3, and 4 suggesting no change in mechanism. It differs from 3 for the Hammett plots for substituent (Z) variations in the leaving group (log k_2 vs. σ_Z) are biphasic concave downwards with breaks at Z = H is interpreted as the change in mechanism.

The reactivity selectivity parameters for 1, 2, 3, 4 are compiled in Table 1 (X= H). and compared. The obtained $\rho_X = -4.35$ to -4.75, and $\beta_X = 0.87$ to 0.95, of 2, ρ_X (= -4.43 to -4.76) and β_X (= 0.88-0.95) for 3, $\rho_X = -5.66$, and $\beta_X = 1.14$ for 4 are somewhat smaller than those in the present work, $\rho_X = -5.78$, and $\beta_X = 1.17$ in 1. The comparable ρ_X and β_X of 1 with those of 2, 3, 4 indicates concerted mechanism for system 1, with a similar but later Transition state structure (TS) i.e., a greater extent of bond-formation in (Fig. 6)

Table 1. Second-Order Rate Constants, k_2 ($\times 10^2$ /M^{-1} s^{-1}) and Selectivity Parameters for the Pyridinolysis of 1, [4-ClPhOP(=O)(4-MePhO)Cl], 2, (YPhO)PhP(=S)Cl, 3, $(PhO)_2P(=O)SPhZ$, 4, (4–ClPhO)PhOP(=O)Cl

Y/X (σ^a [pK_a(pyridines)^b	4-MeO – 0.27 6.47	4-Me – 0.17 6.00	H 0.00 5.17	3-Ph 0.06 4.87	3-Ac 0.38) 3.26]	$-\rho_X$ (^{c}r)	β_X (^{c}r)
4-Me (1, 5.0 °C)	111	23.5	2.62	0.709	0.020	5.78 (0.997)	1.17(0.996)
H (4, 5.0 °C)	121	27.8	3.16	0.918	0.026	5.66(0.997)	1.14 (0.997) [2]
H (2, 35.0 °C)			1.12			4.35 – 4.75^d	0.87 – 0.95^e [4]
H (3, 35.0 °C)			4.42			4.43 – 4.76^f	0.88 – 0.95^g [9]

$^a\sigma$ [11], ^{b}pK_a [12] , ^{c}Correlation coefficients, ^{d} r ≥ 0.994, ^{e} r ≥ 0.988, ^{f} r≥ 0.974, ^{g} r ≥ 0.963

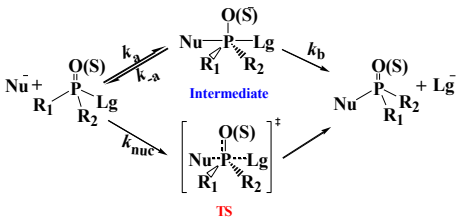


Fig. 1. Schematic representation of S_N reaction at P center

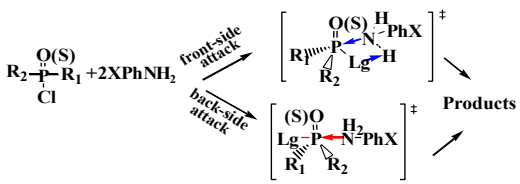


Fig. 2. Schematic representation of nucleophilic attack on P in S_N2

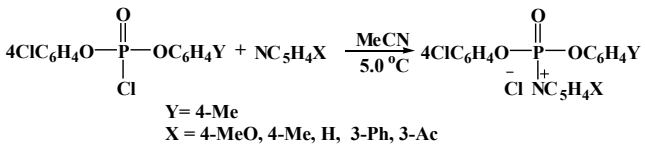


Fig. 3. Reaction systems for the pyridinolysis of 1, in acetonitrile at 5.0 oC (present study)

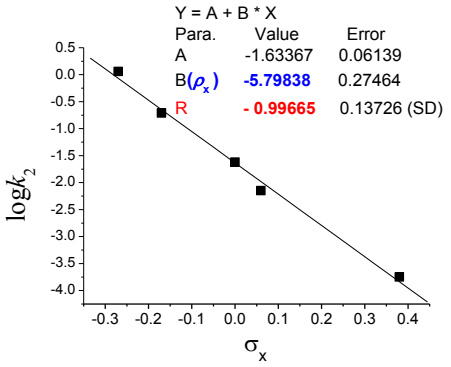


Fig. 4. The Hammett plot for 1.

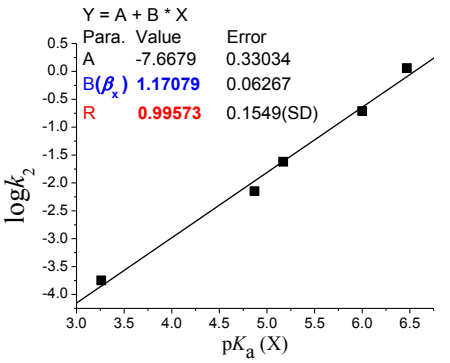
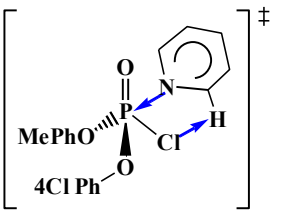


Fig. 5. The Brönsted plot for 1.



TS 1

Fig. 6. Plausible TS structure for 1, where nucleophile attacks from the front side

Acknowledgements

A portion of experimental study was carried out in Chemical Kinetics Laboratory, Inha University, South Korea.

References

[1] Williams A. *Free Energy Relationship in Organic and Bio-Organic Chemistry*. UK: RS.C Press; 2003.

[2] Lumbiny BJ. Effect of substituents on reactivity and reaction mechanism observed in S_N reaction of some organo phosphorus compounds: based on physical organic methodology. *J Asiat Soc Bangladesh Sci* 2012; **38** (1): 17-27.

[3] Adhikary KK, Lumbiny BJ, Dey S, Lee HW. Transition state variation in the anilinolysis of *O*-aryl phenylphosphonochloridethio- ates in acetonitrile. *Bull of Korean Chem Soc* 2011; **32**: 2628.

[4] Lumbiny BJ, Adhikary KK, Lee BS, Lee HW. Pyridinolysis of *O*-aryl phenyl phosphonochloridothioates in acetonitrile. *Bull of Korean Chem Soc* 2008; **29**: 1769-1773.

[5] Lumbiny BJ, Lee HW. Anilinolysis of *S*-aryl phenyl phosphonochloridothioates in acetonitrile. *Bull of Korean Chem Soc* 2008; **29**: 2065-2068.

[6] Adhikary KK, Lumbiny BJ, Lee HW. Kinetics and mechanism of the pyridinolysis of *S*-aryl phenyl phosphonochloridothioates in acetonitrile. *Bull of Korean Chem Soc* 2011; **32**: 3743-3747.

[7] Guha AK, Lee HW, Lee I. Pyridinolysis of phenyl substituted phenyl chlorophosphates in acetonitrile. *J Org Chem* 2000; **65:** 12.

[8] Adhikary KK, Lumbiny BJ, Kim CK, Lee HW. Pyridinolysis of *O*,*O*-Diphenyl *S*-phenyl phosphorothiolates in acetonitrile. *Bull of Korean Chem Soc* 2008; **29**: 851-855.

[9] Hoque MEU, Dey S, Guha AK, Kim CK, Lee BS, Lee HW. Kinetics and mechanism of the aminolysis of the aryl phenyl chlorophosphates with anilines. *J Org Chem* 2007; **72:** 5493.

[10] Hansch C, Leo A, Taft RW. A survey of Hammett substituent constants and resonance and field parameters. *Chem Rev* 1991;**91**: 165-195.

[11] Zuman P, Patel RC. *Techniques In Organic Reactions Kinetics*. U. S. A: John Wiley and Sons; 1984.

[12] Albert A, Serjeant EP. *The Determination of Ionization Constants*. 3rd ed. New York: Chapman and Hall; 1984.